

Potential Health Effects of Space Radiation

*Chui-hsu Yang and +Laurie M. Craise

*NASA Johnson Space Center, Houston, TX 77058

+Lawrence Berkeley Laboratory, Berkeley, CA 94720

ABSTRACT

Crewmembers on missions to the Moon or Mars will be exposed to radiation belts, galactic cosmic rays, and possibly solar particle event. The potential health hazards due to these space radiations must be considered carefully to ensure the success of space exploration. Because there is no human radioepidemiological data for acute and late effects of high-LET radiation, the biological risks of energetic charged particles have to be estimated from experimental results on animals and cultured cells. Experimental data obtained to date indicate that charged particle radiation can be much more effective than photons in causing chromosome aberrations, cell killing, mutation, and tumor induction. The relative biological effectiveness (RBE) varies with biological endpoints and depends on linear-energy-transfer (LET) of heavy ions. Most lesions induced by low-LET radiation can be repaired in mammalian cells. Energetic heavy ions, however, can produce large complex DNA damages, which may lead to large deletions and are irreparable. For high-LET radiation, therefore, there is less or no dose rate effects. Physical shielding may not be effective in minimizing the biological effects of energetic heavy ion, since fragments of the primary particles can be effective in causing biological effects. At present the uncertainty of biological effects of heavy particles is still very large. With further understanding of the biological effects of space radiation, the career doses can be kept at acceptable levels so that the space radiation environment need not be a barrier to the exploitation of the promise of space.

INTRODUCTION

With the success of short-duration space flights, the age for long-term exploration is coming. Along with the long-term space exploration come various potential health hazards due to unique physical factors of space environment. These health hazards must be considered carefully to ensure the success of space exploration. Among the physical factors, ionizing radiation in space is an important one. The risk to crew health from radiation exposure is a major issue of human space flight to the Moon and Mars. The crewmembers of a lunar or Mars mission will be unavoidably exposed to ionizing radiation as they travel through the inner trapped proton belt, the outer trapped electron belt, and through the galactic cosmic rays (GCR) of interplanetary space. In addition, outside of the Earth's magnetosphere, there is the possibility for exposure to charged particle radiation from Solar Particle Event (SPE). These space radiations are different from gamma rays and neutrons

in terms of energy absorption and ionization pattern. Although a significant amount of data on biological effects of gamma rays and neutrons have been obtained from atomic bomb survivors, there is no human radioepidemiological data on bioeffects of charged particle radiation. Therefore, very little biological effects of these space radiations in humans are known, and only limited data have been obtained from research studies with animals and cultured cell systems.

EXPERIMENTAL DATA

Extensive studies on biological effects of heavy ions done in the past decade show that charged particle radiation can be much more effective than gamma rays in causing DNA damage, chromosome aberrations, cell killing, mutation, and tumor (1, 2, 3, 4). The relationship between relative biological effectiveness (RBE) and linear energy transfer (LET) is not a simple one. In general, the RBE increases with LET up to about 100-200 keV/um and then decreases steadily to a value less than 1.0 at very high LET. The peak position of the RBE and LET relationship, however, can vary with different biological endpoints. For a given LET value, the RBE can be different for different effects.

Various biological, chemical, and physical factors can modify the biological responses to gamma rays (Table I). These factors, however, have much less effect on cells irradiated by heavy ions.

Table I. Radiation Responses and Modifiers

Modifier	X or Gamma Rays	High-LET Charged Particles
Dose Rate	effects reduced at low dose rate	effects enhanced or not changed at low dose rates
Cell Cycle	radiosensitivity highly dependent on cell stage	effects less depend on cell stage
Oxygen	radioresistant increases under hypoxic condition	radiosensitivity about the same under hypoxic condition
Radioprotectants	highly effective in reducing radiosensitivity	not very effective in reducing radiation effects
Repair Inhibitors	significantly increase radiosensitivity	not effective in increasing radiation responses

Oxygen concentration, for example, can change RBE value for survival, and extensive studies on oxygen enhancement (OER) have been reported (5). Under hypoxic condition, the RBE at 10% survival level for heavy ions with LETs greater than 100 keV/um can be as high as 5. This increase of RBE value under hypoxic condition is due to the decrease of OER, i.e., oxygen concentration has less effect on radiosensitivity to high-LET charged particles. The calculated cross section for inactivation under aerobic and hypoxic condition increases with an increase of LET and reaches a plateau value close to measured geometry area of cell nucleus.

For high-LET radiation, normal cells in general show higher RBE value than repair deficient cells, suggesting heavy ions effective in producing irreparable lethal lesions (6). The effect of cell cycle on radiosensitivity of cells was found to be diminished with an increase of LET (7), indicating that heavy ions are effective in producing severe DNA damages. Experiments to determine the repair of potential lethal and oncogenic lesions in confluent mouse embryonic cells also showed that the production of irreparable lethal and oncogenic damages was both LET and track structure dependent (8). An analysis of these experimental results indicated that in average more than one heavy particle passing through cell nucleus are needed to inactivate a mammalian cell in culture. Chemical radiation protectants, which can reduce the effect of gamma rays in mammalian cells by several folds, were found to be much less useful for high-LET heavy ions.

Although a significant amount of information on biological effects of heavy ions has been obtained, many biological responses to charged particles remain to be determined. The acute effects on high dose protons on central nervous system, intestine, and bone marrow, for example, are not well known. In addition, most mutagenic and carcinogenic studies were done with cultured cell systems, and very few studies have been done with animals. Furthermore, some unique biological effects of heavy ions, such as microlesions, have been reported although not verified. A summary of experimental data available to date is shown in Table II.

INFORMATION NEEDED FOR REDUCING UNCERTAINTY

The uncertainty of biological data for radiation risk assessment is very large at present. The cause of such uncertainty comes in part from incomplete studies of various biological effects and in part from the limitation of radiation facilities. Most radiobiological studies with charged particles were done with single heavy ion beam at high dose rates, because the cost of using accelerators has been very expensive. In space, crewmembers will be exposed to trapped protons and GCR at very low dose rate. For radiation risk assessment, therefore, it is extremely important to determine the biological effects of charged particles at dose rates comparable to that in space and to study possible synergistic effects of mixed particle radiation.

Because there is no human radioepidemiological data for charged particle radiation, experimental results from research studies have to be extrapolated to

Table II. A Summary of Information on Biological Effects of X or Gamma Rays and Charged Particles.

Biological Endpoint	X or gamma rays	Charged particles
<u>Acute Effects:</u>		
1. Central nervous system	+	limited
2. Intestinal system	+	limited
3. Hemapoietic system	+	limited
<u>Late Effects:</u>		
1. Carcinogenesis		
A) In Vivo	+	limited (most from mouse Harderian gland tumor system)
B) In Vitro	+	+
2. Mutagenesis		
A) In Vivo	+	?
B) In Vitro	+	+
3. Embryogenesis	+	very limited
<u>Unique Effects:</u>		
1. Microlesions		
A) Cornea	-	+(?)
B) Retina	-	+(?)
2. Eye flash	+	+
	(greying of visual field)	(star & streak)

humans for risk analysis. The extrapolation from animal and/or cellular results to humans is a very challenging problem. For example, there are significant difference in radiosensitivity between human fibroblasts and animal cells (10, 11). In addition, human fibroblasts and epithelial cells are much more difficult to be transformed by ionizing radiation, as compared to rodent cells. Multi-exposures are required to change the growth properties of normal human cells, and a single dose can be sufficient to cause neoplastic transformation of rodent cells in culture (12).

There is also tissue and organ specificity in carcinogenesis. All these differences will have to be considered when data from animal and/or cells are extrapolated to humans. One of the possible means to solve this difficult problem is to understand the mechanism(s) of radiation effects, through which biophysical models can be built and used to predict biological responses to charged particles.

Charged particles will be fragmented when they traverse through the body. The biological effects of fragmented heavy ion beams have been studied with only a few ions, and results indicated that an iron beam fragmented by 5- and 7-cm polyethylene can be as effective as the primary particles. More information on the effectiveness of fragmented charged particles in inducing various biological effects are needed for a better risk assessment.

Another source of uncertainty of radiobiological data is microgravity. At present, very little is known how does microgravity alter the radiation responses at cellular, tissue, and organ level. The disturbance of body fluids, hormones, and central nervous system by microgravity may have significant effects on radiation responses. Changes of hormone secretion in the body, for instance, may alter the progression of cancer induced by radiation. Research in this area will have to be performed before one can assess radiation risk with confidence.

CONCLUSION

For a long-term mission to the Moon or Mars, crewmembers will be exposed to charged particles in space. Experimental studies showed that high-LET heavy ions can be much more effective than gamma rays in causing various biological effects, including cell killing, mutation, and carcinogenesis. The relative biological effectiveness of heavy ions depends on LET and varies with different biological endpoints. Although a significant amount of information on biological effects of charged particles has been obtained, much more data on acute as well as late effects of heavy ions are needed for radiation protection. Studies on effects of low dose rate, mixed radiation, microgravity, and mechanisms are essential for reducing the uncertainty of radiobiological data. With further understanding of the biological effects of space radiation, the crewmembers can be better protected to ensure the success of space exploration.

ACKNOWLEDGMENTS

This work was supported by NASA (Contract No. T9297R). The technical assistance of the BEVALAC crews in providing heavy ion beams needed for research studies are gratefully acknowledged.

REFERENCES

1. Cox, R., Thacker, J., Goodhead, D. T., and Munson, R. J. "Mutation and inactivation of cultured mammalian cells by various ionizing radiations" *Nature* (London), 267:425-427 (1977)
2. Blakely, E., Tobias, C. A., Yang, T. C., Smith, K. C., and Lyman, J. T. "Inactivation of human kidney cells by high-energy monoenergetic heavy-ion beams" *Radiat. Res.*, 80:122-160 (1979)
3. Fry, R. J. M., Powers-Risius, P., Alpen, E. L., and Ainsworth, E. J. "High-LET radiation carcinogenesis" *Radiat. Res.* 104:S-188-195 (1985)
4. Yang, T. C., Craise, L. M., Mei, M., and Tobias, C. A. "Neoplastic cell transformation by heavy charged particles" *Radiat. Res.*, 104:S-177-S-187 (1985)
5. Todd, P. W. "Heavy-ion irradiation of cultured human cells" *Radiat. Res. Suppl.*, 7:196-207 (1967)
6. Tobias, C. A., Blakely, E. A., Chang, P. Y., Lomel, L., and Roots, R. "Response of sensitive human ataxia and resistant T-1 cell lines to accelerated heavy ions" *Br. J. Cancer*, 49(Suppl. VI):175-185 (1984)
7. Blakely, E. A., Ngo, F. Q. H., Curtis, S. B., and Tobias, C. A. "Heavy ion radiobiology: cellular studies" *Adv. Radiat. Biology*, 11:295-389 (1984)
8. Yang, T. C., Craise, L. M., Mei, M., and Tobias, C. A. "Neoplastic cell transformation by high-LET radiation: molecular mechanisms" *Adv. Space Res.* 9:131-140 (1989)
9. Yang, T. C., and Tobias, C. A. "Neoplastic cell transformation by energetic heavy ions and its modification with chemical agents" *Adv. Space Res.* 4:207-218 (1984)
10. Yang, T. C., Stampfer, M. R., and Smith, H. S. "Response of cultured normal human mammary epithelial cells to X-rays" *Radiat. Res.* 96:476-485 (1983)
11. Yang, T. C., Stampfer, M. R., and Tobias, C. A. "Radiation studies on sensitivity and repair of human mammary epithelial cells" *Int. J. Radiat. Biology* 56:605-609 (1989)
12. Yang, T. C., Craise, L. M., Prioleau, J. C., Stampfer, M. R., and Rhim, J. S. "Chromosomal changes in cultured human epithelial cells transformed by low- and high-LET radiation" *Adv. Space Res.* 12:127-136 (1992)